

REMARKS/ARGUMENT

Claim Amendments

Claim 1 has been amended to define the composition of matter more particularly.

Claims 3, 4, 6, 7, 9-13, 16, 18, 19, 22, 23, 25, 26, 28, 29, 31, 32 and 34-52 are cancelled without prejudice.

Remaining claims were amended to conform to claim 1.

New claims 58 and 59 are added to narrow the range of PS recited to about 1 to about 45% (w/w).

It is respectfully submitted that no new matter has been added.

Applicant's submissions

General

The present amendment is in response to the Final Office action of March 16, 2010.

Without conceding to any of the Examiner's rejections, this amendment is submitted in order to expedite prosecution of the application.

The claims are amended, as detailed above, and the set of claims now relates to a specific embodiment of the invention – a composition of matter which is a dispersion of an insoluble divalent salt of phosphatidylserine (PS), particularly the calcium and magnesium salts, in an oil base, particularly medium-chain triglycerides, capsules comprising this composition of matter, and the various uses thereof.

Experimental evidence

Applicant respectfully submits herewith a declaration by one of the inventors, Gai Ben-Dror. As detailed in the declaration attached hereto, PS salts which are prepared in a diphasic system are soluble.

As shown in the Gai Ben-Dror declaration, PS salts prepared in various diphasic systems, such as those of De Ferra et al. gave clear solutions when mixed with oils, i.e. were soluble in the oil. Dispersions of such salts in oil could not be prepared, due to their solubility.

The declaration attached hereto is unsigned and an executed declaration with Annex A attached will be submitted as quickly as execution can be obtained.

Claim objections

Claims 21, 24 and 27 were amended in consideration of the Examiner's remarks.

Claim Rejections – 35 USC § 112

The Examiner rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, 30, 33 and 53-57 due to the introduction of the definition "predominantly" in the previous Supplementary Amendment. The claims have been amended by deleting the said definition.

The Examiner further rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, 30, 33 and 53-57 due to the definition of the stability being indefinite. The definition has now been amended to "less than about 5%" decomposition.

The Examiner further rejected claims 55-57 and their dependent claims 2, 5, 8, 14-15, 17, 20-21, 24, 27, 30, 33 and 53-54 as vague and indefinite, due to the definition "nutritional carbohydrates". It is submitted that the term is clear, and encompasses

dietary sugars, polysaccharides, starches, fibers, etc. Nonetheless, without conceding to the Examiner's objection, in order to expedite examination, this term has been amended to recite "carbohydrates".

Novelty

Applicants wish to thank the Examiner for having withdrawn the objections of lack of novelty on record.

Inventive step

The Examiner rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, 30, 33 and 53-57 under 35 USC § 103(a) as being unpatentable over De Ferra et al. (EP 922707) in view of Jorissen et al. (Nutritional Neuroscience, 2002).

The Examiner maintains that De Ferra et al. teach the preparation of PS and its purification by crystallization in the form of the calcium salt, with reference to Examples 1-3 of De Ferra et al., which exemplify the preparation of a purified PS as the calcium salt, from various lecithin sources.

The Examiner further asserts that De Ferra et al. do not teach the incorporation of the PS in a pharmaceutical composition, but that this deficiency is remedied by Jorissen et al.

According to the Examiner, Jorissen et al. describe the administration of PS, admixed with other phospholipids and polyunsaturated fatty acids, encapsulated in a soft gel capsule.

The Examiner therefore states that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of De Ferra et al. with those of Jorissen et al. and utilize the purified PS of De Ferra in a pharmaceutical composition, and one of ordinary skill in the art would have been motivated to do so.

With regard to the storage stability, the Examiner states that although De Ferra et al. is silent, since it is known in the art to utilize oils (MCT) for diluting PS, their use is obvious. Therefore, based on the teachings of De Ferra et al. that the divalent salt of PS is the purer form of PS, there is reasonable expectation that the storage stability would be the same as that instantly claimed.

Applicants respectfully traverse.

De Ferra et al. teach the preparation of PS, and its purification by crystallization as the calcium salt, in a diphasic system. As demonstrated in applicant's attached experimental evidence (Declaration by inventor Gai Ben-Dror, hereafter "the Declaration"), PS calcium salts produced in diphasic systems, such as those taught by De Ferra were soluble in oils. For example, in Section I of the Declaration, Example 2 of De Ferra et al. was repeated. The product and MCT were dissolved in hexane and concentrated under vacuum to give a **clear** PS fluid, indicating that the PS is soluble in oil. The additional examples in the Declaration (Sections II to IV), all further demonstrate that producing PS in a diphasic reaction results in a soluble PS.

As defined in claim 1, the PS composition of matter of the invention is in the form of a **dispersion** of an insoluble divalent metal salt of PS in oil, not a **solution** of PS in oil. This is a major difference, which highly influences the stability of the PS.

In a PS dispersion, molecules on the surface of the dispersed particles are exposed to the surrounding medium (in the present case the oil base) while molecules in the inner part of the dispersed particles are much less exposed to the medium and thus exhibit high stability.

In a PS solution, on the other hand, there are no protected "particles", and thus, the

molecules, being dissolved, are exposed completely to the oil environment and have high decomposition rates.

With particular reference to Jorissen et al., it is respectfully submitted that one of ordinary skill in the art would not have been motivated to combine the teachings of De Ferra with this document, because it is clearly stated that: "*In that article (an earlier work by Jorissen et al.) we concluded that future studies should focus on the way of production of S-PS (soy-PS), because in our studies the S-PS content of the capsules degraded to 50% of the initial value after 15 months.*" (see page 342, penultimate paragraph). The Jorissen et al. reference cited by the Examiner is a mere safety study, and does not remedy this deficiency, because conventional production of S-PS is described. The Examiner assumes that the purified PS obtained by the process of De Ferra should be stable. This is not supported. Even if such assumption was adopted, since Jorissen et al. clearly describe the instability of S-PS, which was in pure form (see page 338, right hand column, "Treatment"), one of ordinary skill in the art would have been taught away from using the pure PS of De Ferra, mixed with oils and encapsulated in a gelatin capsule as in Jorissen, because clearly the PS content would have been substantially degraded. Reference is made to the declaration by Dr. Neta Scheinman, submitted together with the former Amendment, which showed the high storage stability of the PS salt dispersions of the invention, particularly when encapsulated in gelatin capsules.

With regard to claim 21, the comments above are also relevant to this claim.

As to the method claims, the advantages of the PS composition of the invention have been demonstrated during the prosecution of this invention in the past, and above. Therefore, the methods of the invention employing the compositions of matter, food articles and pharmaceutical compositions of the invention are also advantageous, ensuring that a patient receives an effective dose of the PS, which cannot be ensured using the compositions of Jorissen, in which the effective dose is constantly diminished due to

degradation.

The same arguments apply to claim 2 and 55-57 and new claims 58 and 59.

It is therefore respectfully submitted that the invention is not rendered obvious by De Ferra et al. (EP 922707) in view of Jorissen et al. (Nutritional Neuroscience, 2002).

The Examiner further rejected claims 1-2, 5, 8 14-15, 17, 20-21, 24, 27, and 53-57 under 35 USC § 103(a) as being unpatentable over De Ferra et al. (EP 922707) in view of Douglas Laboratories (1999).

De Ferra was addressed by the Examiner as above.

With regard to Douglas Laboratories, the Examiner maintains that this document, which is a data sheet for a dietary supplement discloses a softgel which contains a mixture of phospholipids, inter alia PS, and fatty acids, and also other ingredients such as MCT and soy bean oil. The softgel capsules are designed for supporting the body's nervous system and brain function.

The Examiner maintains that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of De Ferra et al. and of Douglas Laboratories and utilize the purified PS in the pharmaceutical composition of Douglas Laboratories, and one of ordinary skill in the art would have been motivated to do so.

Applicants respectfully traverse.

For the same arguments presented above, the Examiner's conclusion that using the salts of De Ferra in preparing capsules according to Douglas Laboratories should result in encapsulated PS as claimed in the present invention is not founded, and the fact that a salt

is pure does not ensure its properties. The salts of De Ferra would have interacted with the medium, as explained above in respect of Jorissen.

The Examiner further rejected also claims 30 and 33 as being unpatentable over De Ferra et al. in view of Douglas Laboratories and further in view of Geiss (US PG PUB 20040120985).

De Ferra et al. and Douglas Laboratories were addressed as above. With regard to Geiss, the Examiner holds that this document teaches that administration of PS protects against neurons atrophy, normalizes cholesterol/phospholipids ratio in the aging brain, etc.

The Examiner therefore concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of De Ferra et al. in view of Douglas Laboratories and Geiss, and use the PS supplement in a method of enhancing cognitive performance and learning ability as well as improving age-related memory loss, and that the man of ordinary skill in the art would have been motivated to do so.

Applicants respectfully traverse, for all of the reasons detailed above.

Double Patenting

Applicants wish to thank the Examiner for having withdrawn the earlier objections.

In light of the foregoing remarks, this application, it is respectfully urged that the now amended claims should be favorably considered and this amendment entered as placing the application in condition for allowance, or at a minimum, in better form for appeal. Early passage of this case to issue is earnestly solicited. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

It is respectfully requested that, if necessary to effect a timely response, this paper be considered as a Petition for an Extension of Time, time sufficient, to effect a timely response, and shortages in this or other fees, be charged, or any overpayment in fees be credited, to the Deposit Account of the undersigned, Account No. 500601 (Docket no. 7056-X08-020).

Respectfully submitted,

A handwritten signature in black ink that reads "Martin Fleit". The signature is written in a cursive, flowing style.

Martin Fleit, Reg. #16,900

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Attachment: Declaration with Annex A